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Systematic review of spontaneous pneumomediastinum

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A Dissertation Submitted to The Graduate School of
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- ABSTRACT -

Systematic review of spontaneous pneumomediastinum

Spontaneous pneumomediastinum (SPM) is an uncommon disorder with a small number of reported clinical studies. The goal of this study was to investigate the clinical manifestations and natural course of SPM and the currently available treatment options. We retrospectively reviewed 91 patients diagnosed with SPM between January 2008 and June 2015. The mean age of the patients was 22.7 ± 13.2 years, and 67 (73.6%) were male. Chest pain (58, 37.2%) was the predominant symptom. The most frequent precipitating factor before developing SPM was the patient's cough (15.4%), whereas the majority of patients (51, 56.0%) had no precipitating factors. Chest X-ray was diagnostic in 44 (48.4%) patients, and chest computed tomography showed mediastinal air in all cases. Esophagography (10, 11.0%), esophagoduodenoscopy (1, 1.1%), and bronchoscopy (5, 5.5%) were performed selectively due to clinical suspicion, but no abnormal findings that implicated organ injury were documented. Twelve patients (13.2%) were discharged after a visit to the emergency room, and the others were admitted and received conservative treatment. The mean hospital stay was 3.0 ± 1.6 days. There were no complications related to SPM except recurrence in two (2.2%) patients. SPM responds well to conservative treatment and follows a benign natural course. Hospitalization and aggressive treatment can be performed in selective cases.

Key words: Spontaneous pneumomediastinum, Mediastinal emphysema, Outpatient

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I. INTRODUCTION

Pneumomediastinum (PM) is defined as the presence of air or other gas in the mediastinum; it is also known as mediastinal emphysema (Park and Vallières, 2005). It can be categorized as spontaneous PM (SPM) and secondary PM (Park and Vallières, 2005). SPM is a rare and benign disorder that generally occurs in the young adult male without any precipitating factors or disease (Koullias et al., 2004; Park and Vallières, 2005). The hypothesis on the pathogenesis of SPM was described as the Macklin effect in 1944 (Koullias et al., 2004; Park and Vallières, 2005; Sahni et al., 2013). Alveolar rupture might lead to air dissection along the bronchovascular sheaths, finally leading to pulmonary interstitial emphysema that spreads into the mediastinum (Koullias et al., 2004; Takada et al., 2009; Sahni et al., 2013). Secondary PM has a definite precipitating factor such as trauma, a surgical or medical procedure (iatrogenic PM), or infection by a gas-forming organism (Kim et al., 2006; Caceres et al., 2008).

Generally, SPM is considered a comparatively benign disease, but few studies have been published covering substantial data pertaining to SPM (Koullias et al., 2004; Iyer et al., 2009; Takada et al., 2009). Previous reports on SPM are usually case series of small numbers of patients; therefore, the clinical manifestations of SPM have not been fully elucidated due to the rarity of this condition (Iyer et al., 2009). The aim of this study was to document the clinical features and course of SPM and identify the optimal diagnostic methods and treatment by analyzing a large number of patients with SPM.

Ⅱ. MATERIALS AND METHODS

In total, 162 patients with PM were identified during the study period (January 2008 to June 2015). SPM was defined as the radiologic confirmation of air within the mediastinum without any underlying factor. The exclusion criterion was PM with a definite precipitating factor such as trauma, a surgical or medical procedure (iatrogenic PM), or infection. Finally, we retrospectively reviewed 91 patients who were diagnosed with SPM. All medical records of these patients were reviewed with consideration of etiologic factors (age and sex), symptoms, precipitating factors, trigger events, complications, radiologic findings, offered treatment, length of hospital stay, natural course, and outcome. Categorical variables are expressed as percentages, and continuous variables are expressed as mean ± standard deviation. This study was approved by the Institutional Review Board of Ajou University Hospital (MED-MDB-15-268).

Ⅲ. RESULTS

Among the 91 patients with SPM, the mean age was 22.7 ± 13.2 years (range, 12–78), and 67 (73.6%) patients were male. The most frequently reported symptoms were chest pain (58, 37.2%) and cervical pain (28, 17.9%), followed by dyspnea (15, 9.6%), cough (12, 7.7%), and crepitus sensation (10, 6.4%) (Table 1).

Table 1. Patients' symptoms.

Symptoms	Patients, N (%)
Chest pain	58 (37.2)
Cervical pain	28 (17.9)
Dyspnea	15 (9.6)
Cough	12 (7.7)
Crepitus sensation	10 (6.4)
Dysphagia	9 (5.8)
Febrile sensation	7 (4.5)
Back pain	5 (3.2)
Dysphonia	3 (1.9)
Abdominal pain	3 (1.9)
Pharyngeal enlargement	2 (1.3)
Dizziness	1 (0.6)
Rhinolalia	1 (0.6)
Facial swelling	1 (0.6)
General weakness	1 (0.6)

If the patient had more than one symptom, all symptoms were described. The mean white blood cell (WBC) count, percent neutrophils, and C-reactive protein (CRP) were 9,780 ± 2,930/μL, 68.1 ± 10.3%, and 0.5 ± 1.2 mg/dL, respectively. The arterial blood gases were

analyzed in 15 patients who complained of dyspnea. The mean partial pressure of oxygen (PaO_2) was 93.2 ± 24.1 mmHg.

In 51 (56.0%) patients, there was no apparent trigger factor to generate SPM. However, in the remaining 40 (44.0%), there were obvious triggering events. SPM developed most frequently during cough (14, 15.4%). Other factors included diet (13, 14.3%) and physical activity, which was related to the Valsalva maneuver (7, 7.7%) (Table 2).

Table 2. Triggering events.

Triggering events	Patients, N (%)
None	51 (56.0)
Cough	14 (15.4)
Diet	13 (14.3)
Sports (Valsalva maneuver)	7 (7.7)
Vomiting	3 (3.3)
Shouting	1 (1.1)
Working	1 (1.1)
Blowing	1 (1.1)

A medical history predisposing the occurrence of SPM included smoking in 19 (20.9%) patients, recent upper respiratory infection in 7 (7.7%), asthma in 3 (3.3%), and chronic obstructive pulmonary disease in 1 (1.1%). Inhaled therapeutics, which are an established precipitating factor for SPM in Western countries (Koullias et al., 2004; Park and Vallières, 2005; Takada et al., 2009; Sahni et al., 2013), were not used in any of the patients in this study (Table 3).

Table 3. Predisposing conditions.

Condition	Patients, N (%)
Smoking	19 (20.9)
Upper respiratory infection	7 (7.7)
Asthma	3 (3.3)
Chronic obstructive pulmonary disease	1 (1.1)
Drugs	0 (0.0)

Chest X-rays were taken in all patients, and chest computed tomography (CT) was performed in 84 (92.3%) patients. Mediastinal air was observed in 44 (48.4%) patients by chest X-ray and in 100.0% by chest CT. The Macklin effect was observed in 70 (83.3%) patients. Esophagography, esophagogastroduodenoscopy, and flexible bronchoscopy were performed in 10 (11.0%), 1 (1.1%), and 5 (5.5%) patients, respectively. Esophagography and esophagogastroduodenoscopy were performed selectively when esophageal injuries were suspected clinically, and bronchoscopy was done in patients with a suspected bronchial injury on CT. However, the patients did not show any organ injury during further investigation.

Most patients (79, 86.8%) were admitted, whereas 12 (13.2%) refused admission and were discharged after close monitoring in the emergency room. For the patients who were admitted, antibiotics (first-generation cephalosporin) and nasal oxygen were administered as a conservative treatment. The patients fasted due to the possibility of esophageal injury and were allowed to initiate oral intake after showing no clinical symptoms of esophageal injury. The mean hospital stay was 3.0 ± 1.6 days (range, 1–15 days). The mean hospital stay of admitted patients was 3.2 ± 1.6 days, and that of discharged patients at the emergency room was 1 day. The patients were discharged when fully evaluated and became asymptomatic,

even if there were residual radiographic findings of PM. Among the 91 patients, two (2.2%) were readmitted with recurrent SPM (6 months and 9 months after discharge, respectively), and both had an underlying history of asthma.

Ⅳ. DISCUSSION

Pneumomediastinum has been recognized since 1819, and Laennec reported the disease in the case of trauma injuries (Park and Vallières, 2005). SPM was further characterized in a case series by Hamman in 1939 (Koullias et al., 2004; Park and Vallières, 2005; Takada et al., 2009; Sahni et al., 2013). SPM is a rare disease with a reported incidence of less than 1:44,000 (Park and Vallières, 2005; Sahni et al., 2013). The clinical course of SPM has been regarded as benign, and its detailed clinical manifestations and proper treatment strategies have not been fully evaluated due to its rarity. To our knowledge, this study analyzed the largest number of patients with SPM to date.

The clinical presentation of SPM can often be ignored or misdiagnosed because of its vague symptoms (Koullias et al., 2004; Caceres et al., 2008). Most affected patients exhibit some of the typical symptoms, and having a high level of clinical suspicion is necessary for diagnosis (Sahni et al., 2013). Every patient in our series presented with one or more symptoms. Chest pain and dyspnea were the predominant symptoms in our study, which correlates with previous reports mediastinum (Koullias et al., 2004; Caceres et al., 2008; Takada et al., 2009; Sahni et al., 2013; Dajer-Fadel et al., 2014). Other frequently reported symptoms are cervical symptoms including pain, coughing, dyspnea, and dysphagia [(Takada et al., 2009; Dajer-Fadel et al., 2014). Therefore, the initial differential diagnoses are numerous and include pulmonary, cardiac, musculoskeletal, and esophageal etiologies (Caceres et al., 2008). Generally, clinicians can make the differential diagnosis by taking a patient's history and performing a detailed physical examination, electrocardiography, and radiographic or endoscopic studies (Caceres et al., 2008).

The trigger events are mainly associated with the Valsalva maneuver (activity, cough, vomiting, shouting, and inhalation of an illicit drug) (Takada et al., 2009). However, trigger events are not detected in many cases (30%–40%) according to previous reports (Takada et al., 2009; Dajer-Fadel et al., 2014), and our data also showed that more than half of the patients (52, 56.5%) had no definite triggering events. The most remarkable finding of the physical examination was subcutaneous emphysema in many studies (Koullias et al., 2004; Takada et al., 2009; Dajer-Fadel et al., 2014). Hamman's sign, which is generated from the crackles heard with each beat of the heart, is also a well known auscultative sign of SPM (Takada et al., 2009; Sahni et al., 2013; Dajer-Fadel et al., 2014). Fever is also a common finding (Iyer et al., 2009). However, these physical findings of SPM vary among reports (Koullias et al., 2004).

To make a precise diagnosis, imaging needs to be performed (Koullias et al., 2004; Takada et al., 2009; Sahni et al., 2013; Dajer-Fadel et al., 2014). The air itself and an enhanced margin of mediastinal structures can be observed on chest X-rays (Takada et al., 2009). Additionally, some papers have emphasized that when air is present between the sternum and the anterior pericardium or surrounding the pulmonary artery without a lateral film, incorrect diagnosis may occur (Koullias et al., 2004; Takada et al., 2009). Chest X-ray is generally useful for diagnosing PM, although there have been false-negative results (Murayama and Gibo, 2014). In our data, chest X-ray was diagnostic in only 45 (48.9%) patients. Chest CT is more useful than chest X-ray because thin slices are obtained and may reveal other findings such as pulmonary disease that could generate secondary PM (Murayama and Gibo, 2014). Using chest CT, clinicians could rule out cases involving any pathologic findings in the lung such as bullae, blebbing, bronchiectasis, and tuberculosis

scarring. On CT, the Macklin effect appears as linear collections of air in the bronchovascular sheaths (Murayama and Gibo, 2014). The Macklin effect is often seen on CT in patients who have suffered blunt chest trauma, although the Macklin effect has also been reported in CT of patients with SPM (Murayama and Gibo, 2014). Indeed, 70 (83.3%) patients showed the Macklin effect on CT in our series. Therefore, chest CT has to be performed in all cases if SPM is suspected. Further diagnostic tools such as esophagography, esophagoduodenoscopy, or bronchoscopy can be performed when there is high suspicion of an injury of the esophagus or trachea with clinical symptoms such as fever, sweating, leukocytosis, or continuously increasing PM (Dajer-Fadel et al., 2014). However, many reports did not find any clear benefit of these diagnostic modalities, and routine use of these studies should be avoided (Koullias et al., 2004; Kim et al., 2006; Caceres et al., 2008; Iyer et al., 2009; Takada et al., 2009; Dajer-Fadel et al., 2014) they should only be performed in cases with any diagnostic doubt (Koullias et al., 2004; Iyer et al., 2009). Based on our experience, chest CT could be a routine diagnostic imaging modality for PM.

Bed rest and conservative management, such as prophylactic use of analgesics and antibiotics and limitation of oral intake, are indicated in patients with SPM (Koullias et al., 2004; Takada et al., 2009; Dajer-Fadel et al., 2014). Fasting and antibiotics help to prevent mediastinitis by visceral organ perforation (Koullias et al., 2004; Takada et al., 2009; Dajer-Fadel et al., 2014), but are unnecessary for patients without a strong clinical suspicion such as severe symptoms or high levels of inflammatory markers (Koullias et al., 2004; Takada et al., 2009; Dajer-Fadel et al., 2014). Oxygen therapy, so-called “nitrogen washout,” accelerates the disappearance of mediastinal gas by increasing the diffusion pressure of nitrogen in the interstitium (Takada et al., 2009; Sahni et al., 2013). However, many papers

have reported that this intervention is also not conclusive, unlike in pneumothorax, so routine use of oxygen therapy is not recommended (Koullias et al., 2004; Takada et al., 2009; Dajer-Fadel et al., 2014).

Many papers argue that admission and prompt evaluation [(Koullias et al., 2004; Chon et al., 2006; Kim et al., 2006; Caceres et al., 2008; Takada et al., 2009; Moon, 2010; Sahni et al., 2013; Dajer-Fadel et al., 2014) should be performed to allow treatment of SPM, but we consider that it could be treated without aggressive intervention or hospitalization if patients are carefully selected. These patients could be followed as outpatients. Most patients were in their teens, twenties, and thirties; had no medical history; and were safely discharged within a few days without complications. In addition, 12 (13.2%) patients who refused admission and were treated in outpatient clinics also had no complications. An aggressive diagnostic work-up and admission are required if underlying disease or organ dysfunction is strongly suspected. Because of this problem, most of the studies to date consider that admission and evaluation are necessary. However, we believe that patients with no definite clinical symptoms that suggest organ injury could be evaluated minimally and treated in outpatient clinics to save medical resources. Indeed, 50% of patients with SPM were followed as outpatients in one study, none of whom showed exacerbation or future recurrence (Koullias et al., 2004). The reason for admission is to control severe symptoms such as continuous cough, associated infections, treatment of pneumothorax, and evaluation of suspected infection. Patients who do not have complications were discharged in this study (Koullias et al., 2004). Taking into consideration the benign course of SPM, hospitalization has to be considered when diagnosis is in question, the underlying disease needs specific treatment, or an esophageal or tracheal perforation cannot be ruled out.

This retrospective study has shown unique findings compared with previous reports. First, in terms of precipitating factors of SPM, drug abuse has been regarded as the cause of SPM; SPM can occur due to the direct toxic action of heat and the strong vasoconstrictive action of the inhaled substances (Koullias et al., 2004; Takada et al., 2009). However, no drug abusers were enrolled in our study. Second, recurrence of SPM is very rare, reportedly ranging from 0.0% to 1.5% [(Koullias et al., 2004; Chon et al., 2006; Kim et al., 2006; Caceres et al., 2008; Iyer et al., 2009; Dajer-Fadel et al., 2014). Our recurrence rate, 2.2%, was slightly higher than that in previous reports. Two patients showed recurrence of SPM at 13 months and 25 months after the initial SPM, and both of them had an underlying asthma history. Previous research on SPM recurrence reported that such patients usually have comorbidities such as gastrointestinal ulcers, diabetes mellitus, alcoholism, mental retardation, or asthma (Natale et al., 2012). Despite the benign clinical course of SPM, patients with comorbidities have to be informed about the possibility of recurrence of SPM.

Ⅴ. CONCLUSION

SPM is a rare benign disease that presents primarily in young adults who generally make an uneventful recovery. Therefore, in the absence of a concomitant symptoms or severe illness requiring inpatient care, hospitalization and aggressive treatment approaches should be limited and individualized. But diagnosis is in question, the underlying disease needs specific treatment or an esophageal or tracheal perforation cannot be ruled out, we should take into acount hospital treatment. To avoid the potentially catastrophic complications of secondary pneumomediastinum, a detailed medical history and careful physical examination are required. CT could help to discriminate other cause of pneumomediastinum.

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– 국문요약 –

Systematic review of spontaneous pneumomediastinum

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박 수 진

(지도교수: 임 상 현)

자연성 종격동 기종은 세계적으로 보고된 환자가 많지 않은 드문 양성 질환이다. 이번 연구의 목적은 자연성 종격동 기종의 임상양상 및 자연경과를 평가해보고 현재 치료의 기준을 확립하는데 있다. 2008년부터 2015년까지 아주대학교 병원에서 자연성 종격동 기종으로 진단 받은 91명의 환자를 대상으로 회고적인 연구를 시행하였다. 환자들의 평균 나이는 22.7 ± 13.2세 였고 그 중 67명(73.6%)은 남성 이었다. 흉통이 가장 흔한 증상으로 58명(37.2%)에서 관찰되었다. 가장 흔한 질병 발생 유발요인은 기침(15.4%) 이었지만 대부분의 환자 51명(56.0%)에서는 특별한 유발요인이 없이 발생하였다. 44명(48.4%)의 환자에서 단순 흉부촬영으로 진단이 가능했으나 흉부 전산화 단층촬영에서는 모든 환자의 종격동에서 공기가 관찰되었다. 환자의 증상을 바탕으로 다른 질병을 배제하기 위해 10명(11.0%)에서 식도 조영술, 1명(1.1%)에서 위 식도 내시경검사, 5명(5.5%)에서 기관지 내시경을 시행하였으나 시행한 모든 환자에서 특별한 이상소견은 관찰되지 않았다. 12명(13.2%)의 환자는 응급실에 내원하여 진단 받은 이후 바로 귀가하였고 그 외의 모든 환자는 입원하여 보존적인 치료를 받았다. 환자의 평균 재원기간은 3.0 ± 1.6일 이었다. 자발성 종격동 기종이 재발한 2명(2.2%)의 환자를 제외

한 다른 합병증은 없었다. 자발성 종격동 기종은 보존적인 치료로 특별한 합병증 없이 치유되는 양성질환으로 정확하게 진단이 된 환자에 있어서는 입원 및 적극적인 검사는 제한적으로 시행되어야 할 것으로 사료되며 입원치료 보다는 외래를 통한 추적관찰이 필요한 양성질환으로 사료된다.

Key words: 자발성 종격동 기종, 종격동 공기증, 외래환자